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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,464	02/14/2006	Kristofer Olofsson	059490-5048-US	1368

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EXAMINER	
COPPINS, JANET L	

ART UNIT	PAPER NUMBER
1626	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,464	OLOFSSON ET AL.	
	Examiner	Art Unit	
	JANET L. COPPINS	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33 and 35-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-31, 39-42* is/are allowed.

6)☒ Claim(s) *32,33 and 35-38* is/are rejected.

7)☒ Claim(s) *35* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/29/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-33 and 35-42 are now pending in the instant application.

Information Disclosure Statement

2. Applicants' Information Disclosure Statement (IDS), submitted September 29, 2008,

Response to Amendment

3. Applicants' Amendment and Response of September 29, 2008, has been reviewed by the Examiner and entered of record in the file. Accordingly, claim 34 has been cancelled, and claims 1, 2, 35, 37, 38, 40 and 41 have been amended.

4. The Examiner notes with appreciation the deletion of the non-elected subject matter from the claims.

Previous Claim Rejections –

35 USC § 112

5. Claims 1, 2, 14, 37, 38, 40 and 41 previously rejected under 35 USC 112, second paragraph, as being indefinite.

(a) Claims 1 and 40 rejected for reciting "spacer group." Applicants have deleted this terminology from the claims, thereby rendering the rejection moot.

(b) Claims 2, 14, 40 and 41 were rejected for reciting definitions for "Z" with no antecedent basis. In view of Applicants' amendments to claim 1 in order to better define "Z," the rejection is overcome and is withdrawn.

(c) Claims 37 and 38 previously rejected for reciting a compound "as defined above." Applicants have amended the claims such that they now depend from claim 1, therefore the rejection is withdrawn.

6. Claims 32-25 previously rejected under 35 USC 112, first paragraph, as not being enabled. Applicants have cancelled claim 34, and amended claims 32, 33 and 35 such that they are directed to methods of inhibiting the activity of mPGES-1 by administering a compound of claim 1 to a host in need thereof. While Applicants have deleted the treatment of specific diseases from the claims, the disclosure still fails to enable the *in vivo* administration of a compound of claim 1, as recited in claims 32, 33 and 35.

As Examiner Barker stated in the previous Office Action, Applicants have not provided any support for treating specific diseases via the administration of the instant claimed compounds, nor does the Specification provide enabling support for *in vivo* administration. Applicants provide *in vitro* mPGES-1 inhibition data in one single assay on pages 49-50 of the Specification, and no further working examples. Thus, Applicants have provided support for the claimed compounds' ability to inhibit mPGES-1 *in vitro*. As argued in the previous Office Action, the greatly increased complexity of the *in vivo* environment as compared to the very narrowly defined and controlled conditions of an *in vitro* assay does not permit a single extrapolation of *in vitro* assays to human diagnostic efficacy with any reasonable degree of predictability. In view of the lack of evidenciary support, the Examiner recommends amending claims 32 and 25 such that they are directed to a method of inhibiting the activity of mPGES-1 *in vitro*, and cancelling claim 33. Claims 32, 33 and 35 remain rejected as not being enabled.

New Claim Rejections-

35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 36-38 rejected under 35 U.S.C. 112, first paragraph, as not being fully enabled. While various active ingredients may be listed in the specification, the claims are not enabled for *any* "therapeutic agent that is useful in the treatment of inflammation," since there is no indication as to the full range of "therapeutic agent[s]" that could be utilized.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The nature of the invention

The nature of the invention is a "combination product," containing a compound of claim 1 and an additional "therapeutic agent that is useful in the treatment of inflammation."

The state of the prior art and the predictability or lack thereof in the art

It is well recognized in the medical art that treatment of diseases or symptoms are not analogous terms. The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. Also, in the absence

of a showing of correlation between *all* of the potential therapeutic agents encompassed by claims 36-38 and the compound of claim 1, one of skill in the art is unable to fully predict possible results from the administration of the claimed compounds.

The amount of direction or guidance present and

the presence or absence of working examples

Treatment of specific diseases or disorders is normally disease or symptom oriented, thus are highly individualized, i.e. a composition for treating inflammatory joint pain would not employ the same agents (requires an additional NSAID agent) as a composition for treating inflammatory bowel disease (requires an additional 5-ASA). If Applicants allege that treating said disorders benefit from inhibiting mPGES-1, then Applicants must demonstrate that a composition for inhibiting the biochemical pathway of mPGES-1 and all of the possible combinations of compositions of claims 36-38 are inexorably linked. Applicants have provided no support whatsoever in the Specification for the additional "therapeutic agents" recited, other than the brief mention on page 47 of "NSAIDS and coxibs." The efficacy of a pharmaceutical composition intended for treatment of a specific disease/disorder needs to be specifically and individually supported by factual evidence. The data provided in the disclosure is insufficient evidence for all possible compositions claimed. A disclosure should contain representative examples, which provide reasonable assurance to one skilled in the art that compounds fall within the scope of a claim will posses the alleged activity. See *In re Riat* et al. (CCPA 1964) 327 F2d 685, 140USPQ 471; *In re Barr* et al. (CCPA 1971) 444 F 2d 349, 151 USPQ 724.

The breadth of the claims

Applicants are claiming a "combination product" containing a compound of claim 1 and

an additional "therapeutic agent." The argument that the agents claimed by the Applicants are dependent upon the disease being treated is insufficient support that the Applicants are enabled for all inflammatory agents, etc.

The quantity of experimentation needed

The quantity of experimentation needed is undue. One of ordinary skill in the art without direction, would be unable to test each and every combination encompassed by claims 36-38. One of skill in the art would need to determine whether the claimed composition would provide treatment of all the inflammatory conditions intended, and there are certainly hundreds of combinations of compositions encompassed by the claim. Based on the unpredictable nature of the invention and the state of the prior art and the breadth of the claims, one of ordinary skill in the art would be burdened with undue "experimentation study" to determine whether the claimed "combination product" would in fact treat the targeted disorder.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds and agents exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad recitation of any or all additional agents, etc of claims 36-38. As a result, necessitating one of skill to perform an exhaustive search for which claimed compositions can be utilized.

The Examiner suggests claiming some specific agents that are enabled by the

Specification or in literature, and to provide support for the recited "combination product."

Claim Objections

9. Claim 35 objected to under 37 CFR 1.75 as being a substantial duplicate of claim 32. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Conclusion

10. In conclusion, claims 1-33 and 35-42 are pending in the instant application. Claims 1-31 and 39-42 appear allowable over the prior art, claims 32, 33 and 35-38 are rejected, and claim 35 is also objected to.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JANET L. COPPINS whose telephone number is (571)272-0680. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571.272.0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/REI-TSANG SHIAO /

Janet L. Coppins
January 13, 2009

REI-TSANG SHIAO
Primary Examiner, Art Unit 1626